LUPINE PUBLISHERS

Current Trends in Gastroenterology and Hepatology

DOI: 10.32474/CTGH.2022.03.000163

ISSN: 2641-1652

Mini Review

Pathological Aspect following Neoadjuvant Radiotherapy in Locally Advanced Rectal Cancer

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Received: December 16, 2021 **Published:** January 11, 2022

Abstract

In locally advanced rectal cancer (LARC), neoadjuvant radiotherapy (RT) is usually performed. RT can avoid an aggressive operation and colostomy creation and can preserve the function of the anus. And various clinical trials for additional treatment, such as immunotherapy, which has recently attracted attention, after RT are being made. In rectal cancer, it is known that it is associated with mutational burden and MSI status rather than PD-L1 expression. Therefore, it is necessary to pay close attention to the pathological changes after RT to predict the efficacy of additional treatment after RT or to find a method for immune modulation for immunotherapy to work effectively.

Assessment of Post-Radiation Tumor Reduction and Sampling

First, the entire tumor volume is obviously reduced. Extravasated mucin, thickened and hyalinized vasculature was often observed. Compared to chemotherapy, which transforms into significant eosinophilic cytoplasm or bizarre morphology, the morphologic change of the tumor cell due to RT is slight. Because the operation is performed several weeks after RT, the tumor portion is replaced by dense fibrotic tissue and often regenerating surface epithelium rather than young fibroblasts. Because of only a tiny number of scattered tumor nests exist, it is difficult to confirm the remaining tumor tissue after RT for research grossly, even an experienced pathologist. So, it is so challenging to collect fresh tissue from an appropriate site. To proceed with research using the remaining tumor tissue after RT, it is appropriate to use formalin-fixed paraffin-embedded tissue as a laser dissection method through microscopic review. Alternatively, it is not easy to distinguish it from normal tissue, even using specific markers if fresh tissue is used. It is necessary to make a slide with the tissue on the mirror side and check whether there is a tumor or not. The evaluation of treatment responsiveness after radiotherapy is made by pathologic examination. The widely accepted tumor regression grade (TRG) is the American joint committee on cancer system, Mandard, and Dworak [1].

Tumor Budding after RT

Tumor budding is a unique tumor pattern known as one aspect of the epithelial mesenchymal transition of colorectal cancer. After RT, it is difficult to evaluate tumor budding because of the sparsely present tumor cells in a small number. However, there is a report that tumor budding of residual rectal cancer in post-RT samples is also related to prognosis such as overall survival. Loss of cohesiveness, that is, tumor budding, is related to nodal metastasis, the evaluation of tumor budding after RT was also related to disease specific recurrence in the pattern that appeared or remained after RT [2]. In the sample that received RT, it was evaluated into clusters of 4 or less tumor cells and 3-tiers - low, intermediate, and high, in the same way as the method for measuring tumor budding in general [3, 4].

Post-RT Immune Cell Infiltration and Components

Rectal cancer is a tumor with an active immune response than any other cancer. In post-RT surgical specimens, it is usually observed that immune cells are reduced, but in the early stage of RT, many inflammatory cells are thought to infiltrate as an inflammatory response. Immunoscore has also been evaluated a lot, and since TIL is known as a prognostic factor [5], it is necessary to evaluate the immune cell population after RT in the future.

Tumor Stroma in the post RT Specimen

In many studies, as an extracellular matrix, tumor stroma has been shown to affect tumor invasion and metastasis [6]. Generally, stroma-rich tumors are resistant to immunotherapy. In addition, it has been reported that stromal maturity can be used as a significant prognostic marker in a large number of cohorts in rectal cancer [7]. However, evaluation studies on the changes in stroma around the tumor after RT are not yet available.

Conclusion

Analysis of changes in the tumor surrounding microenvironment after RT will be a key to predicting the efficacy of RT and its combination therapy for chemotherapy and immunotherapy.

References

1. Kim SH, Chang HJ, Kim DY, Park JW, Baek JY, et al. (2016) What Is the Ideal Tumor Regression Grading System in Rectal Cancer Patients after Preoperative Chemoradiotherapy? Cancer Res Treat 48(3): 998-1009.
2. Jager T, Neureiter D, Fallaha M, Schredl P, Kiesslich T, et al. (2018) The potential predictive value of tumor budding for neoadjuvant chemoradiotherapy response in locally advanced rectal cancer. Strahlenther Onkol 194(11): 991-1006.
3. Koelzer VH, Zlobec I, Lugli A (2016) Tumor budding in colorectal cancer--ready for diagnostic practice? Hum Pathol 47(1): 4-19.
4. Lugli A, Kirsch R, Ajioka Y, Bosman F, Cathomas G, et al. (2017) Recommendations for reporting tumor budding in colorectal cancer based on the International Tumor Budding Consensus Conference (ITBCC) 2016. Mod Pathol 30(9): 1299-1311.
5. Pages F, Mlecnik B, Marliot F, Bindea G, Ou FS, Bifulco C, et al. International validation of the consensus Immunoscore for the classification of colon cancer: a prognostic and accuracy study. Lancet 391(10135): 2128-2139.
6. Conti J, Thomas G (2011) The role of tumour stroma in colorectal cancer invasion and metastasis. Cancers (Basel) 3(2): 2160-2168.
7. Ueno H, Jones AM, Wilkinson KH, Jass JR, Talbot IC (2004) Histological categorisation of fibrotic cancer stroma in advanced rectal cancer. Gut 53(4): 581-586.

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